DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 1, 2005 has been entered.

Claims 24-27, 29, and 30 have been cancelled.

Claims 32-34 have been added.

Claims 1-10, 28, 30, and 32-34 are pending and are under examination in this Office Action.

Applicant is thanked for updating the first line of the specification to indicate that application 09/265,690 has issued as US Patent No. 6,372,440.

Information Disclosure Statement

2. Applicant's IDS received September 15, 2005 is acknowledged and has been considered.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Specifically, applicant is prosecuting claims drawn to antibodies, yet the title only indicates generic methods. One potential title that is more descriptive is "Antibodies for use in detecting deficient cellular membrane tightly bound magnesium for disease diagnoses." Other titles are possible.

The abstract is objected to because it only contains generic statements about the methods disclosed in the specification and does not discuss antibodies, the subject of the claims currently under examination. Amending the abstract to include the instant claimed subject matter is appropriate and required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claim 31 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been rendered moot by the cancellation of said claim.

6. Claims 1, 2, 7-10, 28, and 30 stand rejected and new claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that specifically binds the peptide consisting of SEQ ID NO: 1 and SEQ ID NO: 4 and a hybridoma secreting such an antibody, does not reasonably provide enablement for an antibody that specifically binds the peptide consisting of SEQ ID NO: 2 or a hybridoma that secretes an antibody that binds the peptide consisting of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims for the reasons of record set forth in the office actions mailed October 4, 2004 and reiterated in the office action of April 1, 2005.

Applicant's arguments filed September 1, 2005 have been fully considered but they are not persuasive. Applicant has argued that only routine experimentation would be required to generate an antibody that binds to a peptide consisting of SEQ ID NO:2. SEQ ID NO:2 is a tetrapeptide that is completely contained within the larger pentapeptide of SEQ ID NO:1. SEQ ID NO:4 is degenerate pentapeptide that contains SEQ ID NO:1 and the sequence FVGLM. Applicant argues that it was recognized in the art that epitopes are often comprised of only 4 or 5 amino acids, and that only routine screening would be required to find an antibody that had the ability to bind to a tetrapeptide consisting of SEQ ID NO:2. The examiner agrees that antibodies may be able to bind a linear peptide epitope that consists only of four amino acids, and as such tetrapeptides can be *antigenic*. However, it is not routine in the art to make antibodies

using such a short peptide sequence since as taught by Harlow et al. (of record), the smallest synthetic peptide sequence that consistently elicits an antibody response (and hence is *immunogenic*) is 6 amino acids in length, with approximately 10 amino acids being preferred. As such, it is routine to raise antibodies against a larger immunogenic polypeptide and then map the antibody binding to a smaller antigenic peptide sequence. As has been stated in the rejections of record, Couraud et al. (J Neurochem, 1987, 49:1708-1719, of record, see entire document) performed standard, art recognized procedures described by Harlow et al. in generating their antibodies. Specifically, they teach polyclonal and monoclonal antibodies that were generated using the 11 amino acid neuropeptide substance P (SP), and they mapped the binding of these reagents to smaller polypeptide sequences. Their data indicated that while antibodies that bind a pentapeptide consisting of SEQ ID NO:1 were readily observed (the polyclonal serum and 5 out of 5 distinct monoclonal antibodies), no reactivity was observed to the tetrapeptide consisting of SEQ ID NO:2. The lack of binding in the polyclonal serum is particularly noteworthy, since it indicates that antibodies with the requisite binding specificity are not readily generated.

Given that the application does not disclose a working example of the claimed antibodies that are raised against such a small polypeptide sequence, that antibodies that bind some but not all SP fragments as taught by Couraud et al. were generated using standard, art recognized techniques, that while it is known that antibodies can bind small linear peptides, such as a peptide consisting of 4 amino acids, it is not routine to generate antibodies using such small sequences as an immunogen as taught

by Harlow et al., and since the specification does not indicate that anything other than standard art recognized procedures are required to make an antibody that binds a tetrapeptide consisting of SEQ ID NO:2, it does not appear that a skilled artisan would be able to make and use the full breadth of applicant's claimed invention, especially in the absence of evidence to the contrary. Therefore the rejection of record is maintained.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
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> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 28, and 30 stand rejected under 35 U.S.C. 102(b) as being anticipated by Couraud et al. (J. Neurochemistry, 1987, 49:1708-1718, of record, see entire document) for the reasons of record as set forth in the Office action mailed October 4, 2004.

Applicant's arguments filed September 1, 2005 have been fully considered but they are not persuasive. Applicant argues that the way in which the antibody is made alters its structure and that such an alteration in structure makes claimed antibodies different from the prior art and as such the rejection should be withdrawn.

The structure required of the product recited in the indicated claims must a) be an antibody and b) bind a peptide consisting of either SEQ ID NO:1, SEQ ID NO:4, or

both SEQ ID NO:1 and 4. Couraud et al. teach products that are a) antibodies (both monoclonal and polyclonal) and b) bind polypeptides consisting of SEQ ID NOs:1 and 4 (see entire document, particularly Table 3, and note that SEQ ID NO:1 is a species of the genus of peptides encompassed by SEQ ID NO:4). This information was communicated to applicant in the office action mailed October 4, 2004, and was restated in the action mailed April 1, 2005.

Applicant argues that a skilled artisan would anticipate that the structure of an antibody will vary depending upon how the antibody is generated, and that the epitope recognized by the monoclonal antibodies of Couraud et al. are likely formed by non-contiguous amino acids which are partially or wholly disrupted by the fragmentation process (see the paragraph that spans pages 9 and 10 of applicant's reply received 9/1/05). The data presented in table 3 of Couraud et al. clearly demonstrates that their monoclonal antibodies bind a peptide consisting of the 5 amino acids of SEQ ID NO:1 and as such the epitope recognized by the antibodies of Couraud et al. consists of the contiguous linear peptide of SEQ ID NO:1. As such, the epitope recognized by the antibodies of Couraud et al. and the epitope recognized by the instant claimed antibodies is the same epitope, namely SEQ ID NO:1.

Applicant continues the argument by indicating that the hypervariable regions of an antibody raised against tetra- and pentapeptides would have distinct hypervariable regions from those of Couraud et al. Applicant is correct that Couraud et al. is silent as concerning the sequences of the hypervariable regions of their antibodies, but applicant is reminded that a) the instant claims do not recite hypervariable region sequences and

b) no data or evidence concerning the hypervariable regions of the claimed antibodies is present in the specification or in any declaration, so it is not possible to determine if the hypervariable sequences are indeed different since the specification does not teach that the claimed antibodies were ever made. Applicant is reminded that the arguments of counsel cannot substitute for evidence where evidence is necessary. See MPEP 2145.

Therefore the rejection of record is maintained.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 9, 2005

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